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Requester's Full Name: L. Eric Crane Examiner #: 65753 Date: 09/28/04
Art Unit: 1623 Phone Number: 272-0651 Serial No. 10/657,762
Mail Box & Bldg/Room Loc: 5D-35 Results Format Preferred: PAPER
[5C-18/Remsen]

If more than one search is submitted, please prioritize searches in order of need.

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Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, key words, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known. Please attach a copy of the cover sheet, pertinent claims, and/or abstract..

Title of Invention: See attached copy of claims.
Inventors (please provide full names): See attached copy of claims.
Earliest Priority Filing Date: 09/09/2002
**For Sequence Searches only* Please include all of the pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

Please search for the compounds of claim 1. See claims 6-17 for specifc compounds.

Please also search for diseases (cls. 24-26 list alternatives including "cancer" and "neutropenia") treated by administration of a compound of claim 1.

Please also search the patent and NON-patent literatures using the inventor name(s).

12
5
33

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Point of Contact:
Alexandra Waclawiw
Technical Info. Specialist
CM1 6A02 Tel. 308-4491

Searcher: _____
Searcher Phone #: _____
Searcher Location: _____
Date Searcher Picked Up: 9-30-04
Date Completed: 9-30-04
Searcher Prep & Review Time: 18
Clerical Prep Time: _____
Online Time: 28

Type of Search

NA Sequence(#) _____
AA Sequence(#) _____
Structure (#) 1
Bibliographic _____
Litigation _____
Full Text _____
Patent Family _____
Other _____

Vendors/cost as applicable

STN 1264 10-21
Dialog _____ PQ
Questel/Orbit _____ Q 12
Dr. Link _____ 12
Lexis/Nexis _____
Seq.Syst'ms _____ 24
WWW/Internet _____ 4
Other(Specify) _____

28

PTO-1590 (11-2003)

Inventor search

Eric Crane 10/657,762

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=> d que  l7
L1          470 SEA "CRISTALLI G"/AU OR "CRISTALLI GLORIA"/AU
L3         2901 SEA ADENOSINE (L) A3 (L) RECEPTOR#
L4           54 SEA L1 AND L3
L7           18 DUP REM L4 (36 DUPLICATES REMOVED)


=> d bib ab ct l7 1-18

L7   ANSWER 1 OF 18  WPIDS  COPYRIGHT 2004 THE THOMSON CORP on STN DUPLICATE 1
AN   2004-282845 [26]   WPIDS
DNC  C2004-108672
TI   New purine derivatives useful as adenosine A3
     receptor agonists for treating e.g. cancer and neutropenia.
DC   B02
IN   CRISTALLI, G
PA   (CRIS-I) CRISTALLI G; (CVTH-N) CV THERAPEUTICS INC
CYC  105
PI   WO 2004022573   A2 20040318 (200426)* EN   44
        RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS
            LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
         W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
            DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
            KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH
            PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG UZ VC VN
            YU ZA ZM ZW
     US 2004121978   A1 20040624 (200442)
     AU 2003268526   A1 20040329 (200459)
ADT  WO 2004022573 A2 WO 2003-US28025 20030908; US 2004121978 A1 Provisional US
     2002-409424P 20020909, US 2003-657762 20030908; AU 2003268526 A1 AU
     2003-268526 20030908
FDT  AU 2003268526 A1 Based on WO 2004022573
PRAI US 2002-409424P      20020909; US 2003-657762      20030908
AB   WO2004022573 A UPAB: 20040421
     NOVELTY - Purine derivatives (I) are new.
          DETAILED DESCRIPTION - Purine derivatives of formula (I) are new.
          R = H or lower alkyl;
          R1 = lower alkoxy or cycloalkyloxy (both optionally substituted);
          R2 = alkyl, cycloalkyl, (hetero)aryl (all optionally substituted), H
     or trialkylsilyl;
          R3 = hydroxymethyl or R4R5NC(O); and
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R4, R5 = alkyl, cycloalkyl (both optionally substituted) or H. INDEPENDENT CLAIMS are also included for:
(1) preparation of (I); and
(2) a method of treating a disease state by stimulating **adenosine A3 receptors.**
ACTIVITY - Cytostatic; Antiasthmatic; Antiinflammatory; Cardiant; Vasotropic; Neuroprotective; Immunostimulant.
MECHANISM OF ACTION - **Adenosine A3 Receptor** Agonist.
Test details are described but no results given.
USE - (I) Are useful in the treatment of a diseases such as cancer, neutropenia (claimed), neurological and cardiac ischemia, asthma, leukopenia and inflammation.
ADVANTAGE - (I) Are selective agonists of **A3 adenosine receptor** and thus avoids side effects caused by interaction with other **adenosine receptors.**
Dwg.0/0

L7 ANSWER 2 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 2
AN 2004:131649 CAPLUS
DN 141:71783
TI A2B Adenosine Receptor Agonists: Synthesis and Biological Evaluation of 2-Phenylhydroxypropynyl Adenosine and NECA Derivatives
AU Vittori, S.; Costanzi, S.; Lambertucci, C.; Portino, F. R.; Taffi, S.; Volpini, R.; Klotz, K.-N.; **Cristalli, G.**
CS Dipartimento di Scienze Chimiche, Universita di Camerino, Camerino (MC), Italy
SO Nucleosides, Nucleotides & Nucleic Acids (2004), 23(1 & 2), 471-481
CODEN: NNNAFY; ISSN: 1525-7770
PB Marcel Dekker, Inc.
DT Journal
LA English
AB In the search for agonists for the elusive A2B adenosine receptor subtypes, 2-phenylhydroxypropynyl-5'-N-methylcarboxamido adenosine (PHPMECA), 2-phenylhydroxypropynyl-5'-N-propylcarboxamido adenosine (PHPPECA), and N6-ethyl-2-phenylhydroxypropynyl-5'-N-ethylcarboxamidoadenosine were synthesized on the basis that introduction of alkynyl chains in 2-position of adenosine derivs. resulted in reasonably good A2B potency compared to NECA [see N6-ethyl-2-phenylhydroxypropynyl adenosine EC50 = 1,700 nM and 2-phenylhydroxypropynyl-5'-N-ethylcarboxamido adenosine (PHPNECA) EC50 = 1,100 nM, resp.]. Radioligand binding studies and adenylyl cyclase assays, performed with recently cloned human A1, A2A, A2B, and A3 adenosine receptors, showed that these modifications produced a decrease in potency at A2B receptor, as well as a general reduction in affinity at the other receptor subtypes. On the other hand, the contemporary presence of an Et substituent in N6-position and of a 4'-ethylcarboxamido group in the same compds. led to (R,S)-N6-ethyl-2-phenylhydroxypropynyl-5'-N-ethylcarboxamidoadenosine and (S)-N6-ethyl-2-phenylhydroxypropynyl-5'-N-ethylcarboxamidoadenosine, which did not show the expected increase in potency at A2B subtype. Hence, (S)-2-phenylhydroxypropynyl-5'-N-ethylcarboxamidoadenosine [(S)-PHPNECA] with EC50 A2B = 220 nM remains the most potent agonist at A2B receptor reported so far.
CT Adenosine receptors
CT Adenosine receptors
CT Adenosine receptors
CT **Adenosine receptors**
CT Structure-activity relationship
CT Human
CT Purine nucleosides

RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 3
AN 2003:467788 CAPLUS
DN 140:35310
TI 9-Ethyladenine derivatives as adenosine receptor antagonists: 2- and 8-substitution results in distinct selectivities
AU Klotz, Karl-Norbert; Kachler, Sonja; Lambertucci, Catia; Vittori, Sauro; Volpini, Rosaria; **Cristalli, Gloria**
CS Institut fuer Pharmakologie und Toxikologie, Universitaet Wuerzburg, Wuerzburg, 97078, Germany
SO Naunyn-Schmiedeberg's Archives of Pharmacology (2003), 367(6), 629-634
CODEN: NSAPCC; ISSN: 0028-1298
PB Springer-Verlag
DT Journal
LA English
AB 9-Ethyladenine was used as the basis for a series of non-xanthine adenosine receptor antagonists at human adenosine receptors. The adenine-based compds. were substituted in 2- or 8-position with a variety of side chains including some aryl or arylalkynyl groups previously tested as 2-substituents in adenosine and 5'-N-ethylcarboxamidoadenosine (NECA) for their effect on agonist affinity. The affinity of the novel compds. was tested in radioligand binding assays (A1, A2A and A3) and inhibition of NECA-stimulated adenylyl cyclase activity (A2B) in membranes prepared from CHO cells stably transfected with the resp. human receptor subtype. High affinity antagonists were identified for A1 (9-ethyl-8-phenyl-9H-adenine, compound 2; 6-(1-butylamino)-9-ethyl-8-phenyl-9H-purine, compound 3), A2A (8-ethoxy-9-ethyladenine; compd.8) and A3 (9-ethyl-8-phenylethynyl-9H-adenine, compound 5) with selectivities vs. other receptor subtypes in the range of 10 to 600. These results demonstrate that adenine is a useful template for further development of high-affinity antagonists with distinct receptor selectivity profiles.
CT Affinity
CT Human
CT Pharmacophores
CT Adenosine receptors
CT Adenosine receptors
CT Adenosine receptors
CT **Adenosine receptors**
CT Structure-activity relationship
RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 4 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 4
AN 2002:931581 CAPLUS
DN 139:32207
TI 2- and 8-alkynyladenosines: conformational studies and docking to human **adenosine A3 receptor** can explain their different biological behavior
AU Costanzi, Stefano; Lambertucci, Catia; Vittori, Sauro; Volpini, Rosaria; **Cristalli, Gloria**
CS Dipartimento di Scienze Chimiche, Universita di Camerino, Camerino, 62032, Italy
SO Journal of Molecular Graphics & Modelling (2003) 21(4), 253-262
CODEN: JMGMFI; ISSN: 1093-3263
PB Elsevier Science Inc.
DT Journal
LA English
AB Adenosine (Ado) derivs. substituted at the C2 position with an alkynyl

chain are endowed with high affinity for A1, A2A and A3 human adenosine receptors, while being less active at the low affinity A2B subtype. On the other hand, the introduction of an alkynyl chain at the C8 position of adenosine is detrimental for the affinity and potency at A1, A2A, and A2B receptors, while is more tolerated by the A3 receptor. The evaluation of the stimulation of [35S]GTPγS binding revealed that 2-alkynyladenosines behave as adenosine receptors agonists while, on the contrary, 8-alkynyladenosines behave as antagonists. With this work we demonstrated, by means of an NMR-based and a computational conformational anal., that 8-alkynyladenosines, differently from 2-alkynyladenosines, cannot adopt the sugar-base anti conformation required for adenosine receptor activation. Furthermore, using the recently reported x-ray crystal structure of bovine rhodopsin as template, we built a 3D model of the seven transmembrane domains of the human adenosine A3 receptor with the homol. modeling. After identification of the binding site we carried out docking expts., demonstrating that the two class of mols. have different binding modes that explain their different degree of affinity and the shift of their activity from agonism to antagonism.

CT Adenosine receptors
CT Adenosine receptors
CT Adenosine receptors
CT **Adenosine receptors**
CT Conformation
CT Human
CT Molecular association
CT Molecular modeling
CT Purinoceptor agonists
CT Purinoceptor antagonists
CT Conformation
RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 5 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 5
AN 2002:457821 CAPLUS
DN 137:155141
TI N6-Alkyl-2-alkynyl Derivatives of **Adenosine** as Potent and Selective Agonists at the Human **Adenosine A3 Receptor** and a Starting Point for Searching A2B Ligands
AU Volpini, Rosaria; Costanzi, Stefano; Lambertucci, Catia; Taffi, Sara; Vittori, Sauro; Klotz, Karl-Norbert; **Cristalli, Gloria**
CS Dipartimento di Scienze Chimiche, Universita di Camerino, Camerino, 62032, Italy
SO Journal of Medicinal Chemistry (2002), 45(15), 3271-3279
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
OS CASREACT 137:155141
AB A series of N6-alkyl-2-alkynyl derivs. of adenosine (Ado) have been synthesized and evaluated for their affinity at human A1, A2A, and A3 receptors and for their potency at A2B adenosine receptor subtypes. The corresponding 2-(1-alkynyl) derivs. of 5'-N-ethylcarboxamidoadenosine (NECA) and Ado are used as reference compds. Binding studies demonstrated that the activities of 2-alkynylAdos were slightly increased for the adenosine A1 receptor and slightly decreased for both A3 and A2B subtypes compared to those of their corresponding NECA derivs., whereas the A2A receptor affinities of the two series of nucleosides were similar. The presence of a Me group on N6 of the 2-alkynyladenosines, inducing an increase in affinity at the human A3 receptor and a decrease at the other subtypes, resulted in an increase in A3 selectivity. In particular,

2-phenylethynyl-N6-methylAdo showed an A3 affinity in the low nano-molar range (Ki(A3) = 3.4 nM), with a A1/A3 and A2A/A3 selectivity of about 500 and 2500, resp. These findings motivated us to search for the preparation of new selective radio-ligands for the A3 subtype; hence, a procedure to introduce a tritiated alkylamino group in these mols. was carried out. As far as the potency at the A2B receptor, the type of 2-alkynyl chain and the presence of the ethylcarboxamido group on the sugar seem to be very important; in fact, the (S)-2-phenylhydroxypropynyl-NECA [(S)-PHPNECA, EC50(A2B) = 0.22 μM] proved to be one of the most potent A2B agonist reported so far. On the other hand, the (S)-2-phenylhydroxypropynyl-N6-ethylAdo [EC50(A2B) = 0.73 μM] showed a significantly increase of potency at the A2B subtype in comparison with the N6-Me, N6-iso-Pr, and the unsubstituted adenosine derivs., although it resulted in being less potent than (S)-PHPNECA [EC50(A2B) = 0.22 μM]. These observations suggest that the introduction of an Et group in the N6-position and an ethylcarboxamido substituent in the 4'-position of (S)-2-phenylhydroxypropynyladenosine could lead to a compound endowed with high potency at the A2B receptor.

CT **Adenosine receptors**
CT **Adenosine receptors**
CT **Adenosine receptors**
CT **Adenosine receptors**
CT Human
CT Structure-activity relationship
CT Nucleosides, preparation
RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

Not in STN

L7 ANSWER 6 OF 18 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 2002412998 EMBASE
TI Purine nucleosides bearing 1-alkynyl chains as adenosine receptor agonists.
AU Volpini R.; Costanzi S.; Lambertucci C.; Vittori S.; **Cristalli G.**
CS G. Cristalli, Dipartimento di Scienze Chimiche, Universita di Camerino, Via S. Agostino 1, 62032 Camerino, Italy. gloria.cristalli@unicam.it
SO Current Pharmaceutical Design, (2002) 8/26 (2285-2298).
Refs: 61
ISSN: 1381-6128 CODEN: CPDEFP
CY Netherlands
DT Journal; General Review
FS 030 Pharmacology
037 Drug Literature Index
LA English
SL English
AB The synthesis and the pharmacological activity of alkynyl derivatives of adenosine (Ado) and N-ethylcarboxamidoadenosine (NECA), that have been tested on adenosine receptors from different sources, have been reviewed. Most of compounds have been characterized in the last ten years by using radioligand binding assays on rat brain membranes and functional studies on different animal models. More recently, the four human adenosine receptor subtypes have been stably transfected into Chinese hamster ovary (CHO) cells allowing for comparative studies in a similar cellular background, utilizing radioligand binding studies (A(1), A(2A), A(3)) or adenylate cyclase activity assays (A(2)B). From the whole pattern of studies the following structure-activity relationships have been drown: The activities of 2-alkynylAdos resulted slightly higher at A(1) and lower at A(3) and A(2B) subtypes than the corresponding NECA derivatives, whereas the affinities at A(2A) subtype are similar for the two series of nucleosides. -The presence of a methyl group on N(6) of the

2-alkynyladenosines, inducing a contemporary increase in affinity at the human A(3) receptor and a decrease at the other subtypes, resulted in a relevant increase in A(3) selectivity. In particular, 2-phenylethynyl-N(6)-methyl Ado showed an A(3) affinity in the low nanomolar range (K(i) A(3) = 3.4 nM), and about 500 fold A(1)/A(3) and about 2500 fold A(2A)/A(3) selectivity. -The presence of a hydroxyl group in some alkynyl side chains led to potent inhibitors of platelet aggegation induced by ADP. -Introduction of particular substituents, such as the racemic 2-phenylhydroxypropynyl group, both in adenosine and in NECA analogues, led to highly potent, non selective agonists at all the four subtypes. -For the potency at A(2B) receptor it seems to be very important the type of alkynyl chain in 2-position and the presence of the carboxyamido group on the sugar; in fact, the (S)-2-phenylhydroxypropynylNECA [(S)-PHPNECA, EC(50) A2(B) = 220 nM] proved to be one of the most potent A(2B) agonist reported so far. -The introduction of alkynyl chain in 8-position of adenosine led to very selective ligands for the A(3) receptor subtype. These nucleosides behave as adenosine antagonists, since they do not stimulate basal [(35)S]GTPγS binding, but inhibit NECA-stimulated binding.

CT Medical Descriptors:
drug synthesis
radioassay
brain membrane
genetic transfection
CHO cell
structure activity relation
receptor affinity
drug selectivity
drug potency
receptor binding
drug structure
drug receptor binding
antihypertensive activity
thrombocyte aggregation inhibition
antioxidant activity
human
nonhuman
rat
animal experiment
controlled study
review
priority journal
Drug Descriptors:
*purine nucleoside derivative: AN, drug analysis
*purine nucleoside derivative: DV, drug development
*purine nucleoside derivative: PD, pharmacology
*adenosine receptor stimulating agent: AN, drug analysis
*adenosine receptor stimulating agent: DV, drug development
*adenosine receptor stimulating agent: PD, pharmacology
adenosine derivative: AN, drug analysis
adenosine derivative: DV, drug development
adenosine derivative: PD, pharmacology
2 hexynyladenosine: AN, drug analysis
2 hexynyladenosine: DV, drug development
2 hexynyladenosine: PD, pharmacology
8 octynyladenosine: AN, drug analysis
8 octynyladenosine: DV, drug development
8 octynyladenosine: PD, pharmacology
8 bromoadenosine: AN, drug analysis
8 bromoadenosine: DV, drug development

8 bromoadenosine: PD, pharmacology
2 iodo n ethylcarboxamidoadenosine: AN, drug analysis
2 iodo n ethylcarboxamidoadenosine: CM, drug comparison
2 iodo n ethylcarboxamidoadenosine: DV, drug development
2 iodo n ethylcarboxamidoadenosine: PD, pharmacology
2 hexynyl n ethylcarboxamidoadenosine: AN, drug analysis
2 hexynyl n ethylcarboxamidoadenosine: CM, drug comparison
2 hexynyl n ethylcarboxamidoadenosine: DV, drug development
2 hexynyl n ethylcarboxamidoadenosine: PD, pharmacology
2 hexynyl n ethylcarboxamidoadenosine: IP, intraperitoneal drug administration
alkynyl group
adenosine receptor: EC, endogenous compound
receptor subtype: EC, endogenous compound
adenosine A1 receptor: EC, endogenous compound
adenosine A2a receptor: EC, endogenous compound
adenosine A3 receptor: EC, endogenous compound
adenosine A2b receptor: EC, endogenous compound
nucleoside derivative: EC, endogenous compound
methyl group
hydroxyl group
adenosine diphosphate: EC, endogenous compound
carboxyl group
phenyl group
adenosine receptor blocking agent: AN, drug analysis
adenosine receptor blocking agent: DV, drug development
adenosine receptor blocking agent: PD, pharmacology
adenylate cyclase: EC, endogenous compound
2 anilinoadenosine: AN, drug analysis
2 anilinoadenosine: DV, drug development
2 anilinoadenosine: PD, pharmacology
adenosine A2a receptor agonist: AN, drug analysis
adenosine A2a receptor agonist: DV, drug development
adenosine A2a receptor agonist: PD, pharmacology
adenosine 5' (n ethylcarboxamide): AN, drug analysis
adenosine 5' (n ethylcarboxamide): DV, drug development
adenosine 5' (n ethylcarboxamide): PD, pharmacology
adenosine A3 receptor agonist: AN, drug analysis
adenosine A3 receptor agonist: DV, drug development
adenosine A3 receptor agonist: PD, pharmacology
neuroleptic agent: CM, drug comparison
neuroleptic agent: PD, pharmacology
superoxide: EC, endogenous compound
unindexed drug
unclassified drug

L7 ANSWER 7 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 6
AN 2001:518628 CAPLUS
DN 135:289005
TI Introduction of alkynyl chains on C-8 of **adenosine** led to very selective antagonists of the **A3 adenosine receptor**
AU Volpini, R.; Costanzi, S.; Lambertucci, C.; Vittori, S.; Klotz, K.-N.; Lorenzen, A.; **Cristalli, G.**
CS Dipartimento di Scienze Chimiche, Universita di Camerino, Camerino, 62032, Italy
SO Bioorganic & Medicinal Chemistry Letters (2001), 11(14), 1931-1934
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal

LA English
AB Some 8-alkynyladenosines were synthesized and evaluated for their adenosine receptor activity, utilizing radio-ligand binding studies (A1, A2A, A3) or adenylyl cyclase activity assays (A2B). Furthermore, the maximal induction of guanosine 5'-(γ-thio)triphosphate ([35S]GTPγS) binding to G proteins and the inhibition of NECA-stimulated binding, in membranes of CHO cells which express the human A3 receptor, were used to determine the intrinsic activity of these nucleosides at the A3 adenosine receptor. The results showed that these new adenosine derivs. are very selective ligands for the A3 receptor subtype and behave as adenosine antagonists, since they do not stimulate basal [35S]GTPγS binding, but inhibit NECA-stimulated binding. This is the first report that adenosine derivs., with unmodified ribose moiety, are adenosine receptor antagonists.
CT **Adenosine receptors**
CT **Adenosine receptors**
CT **Adenosine receptors**
CT **Adenosine receptors**
CT Structure-activity relationship
CT Nucleosides, preparation
RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 8 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 7
AN 2001:675165 CAPLUS
DN 136:20209
TI Synthesis and adenosine receptor affinity and potency of 8-alkynyl derivatives of adenosine
AU Lambertucci, C.; Costanzi, S.; Vittori, S.; Volpini, R.; **Cristalli, G.**
CS Dipartimento di Scienze Chimiche, University of Camerino, Camerino, I-62032, Italy
SO Nucleosides, Nucleotides & Nucleic Acids (2001), 20(4-7), 1153-1157
CODEN: NNNAFY; ISSN: 1525-7770
PB Marcel Dekker, Inc.
DT Journal
LA English
OS CASREACT 136:20209
AB Adenosine derivs. bearing different (ar)alkynyl chains at the 8-position were synthesized and tested at human adenosine receptors. Binding studies showed that all compds. possess affinity for the A3 subtype in the high nM range. Moreover, guanosine 5'-O-(3-[35S]thio)triphosphate binding assay indicated that the 8-alkynyl adenosines behaved as antagonists of NECA at A3 receptors.
CT **Adenosine receptors**
CT Nucleosides, preparation
RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 9 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 8
AN 2001:675007 CAPLUS
DN 136:20202
TI Synthetic procedure for the preparation of novel potent and selective **A3 adenosine receptor** radioligands
AU Volpini, R.; Costanzi, S.; Lambertucci, C.; Vittori, S.; **Cristalli, G.**
CS Dipartimento di Scienze Chimiche, University of Camerino, Camerino, I-62032, Italy
SO Nucleosides, Nucleotides & Nucleic Acids (2001), 20(4-7), 775-779
CODEN: NNNAFY; ISSN: 1525-7770

PB Marcel Dekker, Inc.
DT Journal
LA English
OS CASREACT 136:20202
AB 2-Phenylethynyladenosine and its N6-Me derivative were synthesized and evaluated in binding assays at human adenosine receptors stably transfected on CHO cells. Results showed that the N6-methyl-2-phenylethynyladenosine is endowed with very high affinity and selectivity at A3 receptor subtype. Hence, an alternative procedure for the synthesis of tritiated N6-methyl-2-phenylethynyladenosine was set up to introduce tritiated methylamine in the final step.
CT **Adenosine receptors**
CT Animal cell line
CT Ligands
RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 10 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 9
AN 2000:28935 CAPLUS
DN 132:180801
TI Synthesis of di- and tri-substituted adenosine derivatives and their affinities at human adenosine receptor subtypes
AU Volpini, R.; Camaioni, E.; Costanzi, S.; Vittori, S.; Klotz, K.-N.; **Cristalli, G.**
CS Dipartimento di Scienze Chimiche, Universita di Camerino, Camerino, I-62032, Italy
SO Nucleosides & Nucleotides (1999), 18(11 & 12), 2511-2520
CODEN: NUNUD5; ISSN: 0732-8311
PB Marcel Dekker, Inc.
DT Journal
LA English
AB The synthesis of 2-(hex-1-ynyl)adenosine derivs. substituted at the N6- and/or 5'-position was carried out on the basis that 2-(hex-1-ynyl)adenosine-5'-N-ethyluronamide (HENECA) showed good affinity and different degree of selectivity for rat adenosine receptors. All new compds. were tested in radioligand binding and adenylyl cyclase assays with recently cloned human A1, A2A, A2B, and A3 adenosine receptors.
CT Adenosine receptors
CT Adenosine receptors
CT Adenosine receptors
CT **Adenosine receptors**
CT Structure-activity relationship
CT Receptors
RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 11 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 10
AN 1999:448639 CAPLUS
DN 131:130211
TI Synthesis and receptor affinity of polysubstituted adenosines
AU Vittori, S.; Camaioni, E.; Costanzi, S.; Volpini, R.; Klotz, K.-N.; **Cristalli, G.**
CS Dipartimento di Scienze Chimiche, Universita' di Camerino, Camerino, I-62032, Italy
SO Nucleosides & Nucleotides (1999), 18(4 & 5), 739-740
CODEN: NUNUD5; ISSN: 0732-8311
PB Marcel Dekker, Inc.
DT Journal
LA English
AB In a search for potent and selective adenosine agonists it has been found

that 2-hexynyladenosine-5'-N-ethyluronamide (HENECA) displays high affinity at rat A2A receptor combined with a good A2A vs A1 selectivity. The finding that HENECA shows good affinity also for A3 receptors prompted us to investigate the effect of various substituents in different positions of this mol.

CT Adenosine receptors
CT **Adenosine receptors**
CT Purine nucleosides
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 12 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 11
AN 1999:662445 CAPLUS
DN 131:317333
TI 2-Substituted N-ethylcarboxamidoadenosine derivatives as high-affinity agonists at human **A3 adenosine receptors**
AU Klotz, Karl-Norbert; Camaioni, Emidio; Volpini, Rosaria; Kachler, Sonja; Vittori, Sauro; **Cristalli, Gloria**
CS Institut fur Pharmakologie und Toxikologie, Universitat Wurzburg, Wurzburg, D-97078, Germany
SO Naunyn-Schmiedeberg's Archives of Pharmacology (1999), 360(2), 103-108
CODEN: NSAPCC; ISSN: 0028-1298
PB Springer-Verlag
DT Journal
LA English
AB A number of 2-substituted 5'-N-ethylcarboxamidoadenosine (NECA) derivs. was investigated for their affinity and selectivity at human A3 adenosine receptors. The compds. were tested in radioligand competition studies and modulation of adenylyl cyclase activity on membranes from CHO cell lines stably transfected with the four human adenosine receptor subtypes. In binding studies the most potent compound, 2-(3-hydroxy-3-phenyl)propyn-1-yl-NECA (PHPNECA), exhibited a subnanomolar affinity for A3 adenosine receptors with a Ki value of 0.4 nM. As opposed to the limited A3 selectivity of PHPNECA, a 100-fold selectivity compared to both A1 and A2A receptors was found for 2-(2-phenyl)ethynyl-NECA (PENECA; Ki 6 nM). The EC50 values for activation of adenylyl cyclase via A2A adenosine receptors were in good agreement with the resp. Ki values from binding expts. In contrast, IC50 values for A1 and A3 receptor-mediated inhibition of adenylyl cyclase were shifted to higher values compared to the resp. affinities determined in radioligand competition studies. Similar discrepancies between binding and functional data have been observed for the inhibitory A1 adenosine receptor in previous studies. Therefore, the same A3 selectivity of PENECA compared to A1 receptors was found in binding and adenylyl cyclase inhibition whereas the selectivity compared to A2A receptors that was detected in ligand binding was obscured in the functional assay. The series of compds. presented in this study identifies 2-substitution of the purine system as a promising target for the development of A3-selective high-affinity ligands.

CT **Adenosine receptors**
CT **Adenosine receptors**
CT **Adenosine receptors**
CT **Adenosine receptors**
CT **Adenosine receptors**
CT Structure-activity relationship
RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 13 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 12
AN 1998:496545 CAPLUS
DN 129:260718

TI Synthesis and Biological Activity of a New Series of N6-Arylcarbamoyl, 2-(Ar)alkynyl-N6-arylcarbamoyl, and N6-Carboxamido Derivatives of **Adenosine**-5'-N-ethyluronamide as A1 and **A3** **Adenosine Receptor** Agonists

AU Baraldi, Pier Giovanni; Cacciari, Barbara; Pineda de Infantas, Maria Jose; Romagnoli, Romeo; Spalluto, Giampiero; Volpini, Rosaria; Costanzi, Stefano; Vittori, Sauro; **Cristalli, Gloria**; Melman, Neli; Park, Kyung-Sun; Ji, Xiao-duo; Jacobson, Kenneth A.

CS Dipartimento di Scienze Farmaceutiche, Universita di Ferrara, Ferrara, 44100, Italy

SO Journal of Medicinal Chemistry (1998), 41(17), 3174-3185
CODEN: JMCMAR; ISSN: 0022-2623

PB American Chemical Society

DT Journal

LA English

AB A new series of 1-(6-amino-9H-purin-9-yl)-1-deoxy-N-ethyl-β-D-ribofuranuronamide-bearing N-arylureas or N-arylcarboxamido groups at the purine 6 position and N-arylureas combined with halogens or alkynyl chains at the 2 position (I; R = H, aryl-NHCO, heteroaryl-NHCO; R1 = aryl, aralkyl, aryl-NH, heteroaryl-NH; R2 = H, halo, alkynyl, aralkynyl) have been synthesized and tested for affinity at A1 and A2A adenosine receptors in rat brain membranes and at cloned rat A3 receptors expressed in CHO cells. The derivs. contained the 5' substituent found in the potent, nonselective agonist 1-(6-amino-9H-purin-9-yl)-1-deoxy-N-ethyl-β-D-ribofuranuronamide (NECA). While the carboxamido derivs. I (R = H; R1 = aryl, aralkyl; R2 = H) showed affinity for A1 receptors, the urea derivs. I (R = H, aryl-NHCO, heteroaryl-NHCO; R1 = aryl, aralkyl, heteroaryl; R2 = H) showed different degrees of affinity and selectivity for the A3 adenosine receptor subtype. In particular the derivative bearing a p-sulfonamidophenyl-urea at the 6 position, I (R = R2 = H, R1 = 4-NH2SO2C6H4NH) (II) showed a high affinity (Ki = 9 nM) and selectivity for the A3 receptors compared to that of the reference compound 1-[6-[[(3-iodophenyl)methyl]amino]-9H-purin-9-yl]-1-deoxy-N-methyl-β-D-ribofuranuronamide (IB-MECA). Furthermore, the importance of the stereochem. in the interaction of these ligands at the rat A3 adenosine receptors has been evaluated by introducing a chiral chain at the 6 position. The introduction of halogens or alkynyl chains at the purine 2 position of selected ureas did not give the expected enhancement of potency at A2A and/or A3 receptors but rather showed a dramatic reduction of A2A affinity, resulting in compds. with good A2A/A3 selectivity. For example, the 2-(3-hydroxy-3-phenyl-1-propyn-1-yl)-6-(4-methoxyphenylurea) derivative I [R = H, R1 = 4-MeOC6H4NH, R2 = PhCH(OH)C.tplbond.C] 61 showed the capability to bind simultaneously to A1 and A3 receptor subtypes, excluding the A2A receptor. Compound II was shown to be an agonist, 9-fold more potent than NECA, at A3 receptors in rat RBL-2H3 mast cell membranes through stimulation of binding of [35S]GTP-γ-S.

CT **Adenosine receptors**
CT **Adenosine receptors**
CT Structure-activity relationship
CT Purine nucleosides

RE.CNT 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 14 OF 18 MEDLINE on STN DUPLICATE 13

AN 1998293111 MEDLINE

DN PubMed ID: 9629466

TI New substituted 9-alkylpurines as adenosine receptor ligands.

AU Camaioni E; Costanzi S; Vittori S; Volpini R; Klotz K N; **Cristalli G**

CS Dipartimento di Scienze Chimiche, Universita di Camerino, Italy.

SO Bioorganic & medicinal chemistry, (1998 May) 6 (5) 523-33.
Journal code: 9413298. ISSN: 0968-0896.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199808
ED Entered STN: 19980903
Last Updated on STN: 19980903
Entered Medline: 19980824

AB In the present study an investigation of the structure-activity relationships in 9-ethylpurine derivatives, aimed at preparing A1, A2A, A2B, and **A3** selective **adenosine receptor** antagonists, was undertaken. Our synthetic approach was to introduce various substituents (amino, alkoxy and alkynyl groups) into the 2-, 6-, or 8-positions of the purine ring. The starting compounds for each series of derivatives were respectively: 2-iodo-9-ethyladenine (9), obtained from 2-amino-6-chloropurine (5); 9-ethyl-6-iodo-9H-purine (11), 8-bromo-9-ethyl-adenine (3) and 8-bromo-9-ethyl-6-iodo-9H-purine (13), obtained from 9-ethyl-adenine (2). The synthesized compounds were tested in in vitro radioligand binding assays at A1, A2A, and **A3** human **adenosine receptor** subtypes. Due to the lack of a suitable radioligand the affinity of the 9-ethyladenine derivatives at A2B **adenosine receptors** was determined in adenylyl cyclase experiments. In general, the series of 9-ethylpurine derivatives exhibited a similar pharmacological profile at A1 and A2A **receptors** whereas some differences were found for the **A3** and the A2B subtypes. 8-Bromo-9-ethyladenine (3) showed higher affinity for all **receptors** in comparison to the parent compound 2, and the highest affinity in the series for the A2A and A2B subtypes (Ki = 0.052 and 0.84 microM, respectively). Analyzing the different substituents, a phenethoxy group in 2-position (10a) gave the highest A2A versus A2B selectivity (near 400-fold), whereas a phenethylamino group in 2- and 6-position (10b and 12b, respectively) improved the affinity at A2B **receptors**, compared to the parent compound 2. The presence of a hexynyl substituent in 8-position led to a compound with good affinity at the **A3 receptor** (4d, Ki = 0.62 microM), whereas (ar)alkynyl groups are detrimental for the potency at the A2B subtype. These differences give raise to the hope that further modifications will result in the development of currently unavailable leads with good affinity and selectivity for A2B **adenosine receptors.**

CT Check Tags: Human; Support, Non-U.S. Gov't
Adenylate Cyclase: ME, metabolism
Alkylation
Animals
CHO Cells
Hamsters
Ligands
Magnetic Resonance Spectroscopy
Purines: CH, chemistry
Purines: ME, metabolism
*Purines: PD, pharmacology
Radioligand Assay
*Receptors, Purinergic P1: AG, agonists
Receptors, Purinergic P1: CL, classification
Receptors, Purinergic P1: ME, metabolism
Structure-Activity Relationship

L7 ANSWER 15 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 14
AN 1999:159009 CAPLUS

DN 130:346869
TI Characterization of potent ligands at human recombinant adenosine receptors
AU **Cristalli, Gloria**; Camaioni, Emidio; Costanzi, Stefano; Vittori, Sauro; Volpini, Rosaria; Klotz, Karl-Norbert
CS Dipartimento di Scienze Chimiche, Universita di Camerino, Camerino, I-62032, Italy
SO Drug Development Research (1998), 45(3/4), 176-181
CODEN: DDREDK; ISSN: 0272-4391
PB Wiley-Liss, Inc.
DT Journal
LA English
AB The four adenosine receptor subtypes have been stably transfected into Chinese hamster ovary (CHO) cells allowing for comparative studies in a similar cellular background, using radioligand binding studies (A1, A2, A3) or adenylyl cyclase activity assays (A2B). We are currently using the transfected CHO cells for extensive screening of nucleosides and purine derivs. of our library. Screening of a number of 2-alkynyl analogs of 5'-N-ethylcarboxamidoadenosine (NECA) indicated that introduction of particular substituents, such as the racemic 2-phenylhydroxypropynyl group, led to a highly potent, nonselective agonist at A1, A2, and A3 subtypes (PHPNECA, Ki in the low nanomolar range at the three subtypes). In the A2B functional assay, it has been found that PHPNECA (EC50 A2B = 0.88 μM) is threefold more potent than NECA. This article is the first report in which the introduction of a bulky group in the 2-position of NECA led to a compound that is active as an agonist at the human A2B subtype. On the other hand, the presence of a Ph ring conjugated to the triple bond as in phenylethynylNECA (PENECA) enhanced selectivity for the A3 subtype. In the purine series (potential antagonists), 8-bromo-9-ethyladenine (8-BEA) showed good affinity toward all adenosine receptor subtypes (Ki A1 = 0.28 μM, Ki A2A = 0.052 μM, Ki A2B = 0.84 μM, Ki A3 = 27.8 μM). On the other hand, the introduction of alkynyl chains in the 8-position resulted in an increased affinity at the A3 receptor (8-hexynyl-9-ethyladenine, 8-HEEA, Ki A3 = 0.62 μM and 8-phenylethynyl-9-ethyladenine, 8-PEEA, Ki A3 = 0.086 μM).
CT Adenosine receptors
CT Adenosine receptors
CT **Adenosine receptors**
CT Drug design
CT Drug interactions
CT Drug screening
CT Adenosine receptors
RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 16 OF 18 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 1998:293474 BIOSIS
DN PREV199800293474
TI New high affinity agonists at **A3 adenosine receptors.**
AU Klotz, K.-N. [Reprint author]; Volpini, R.; Vittori, S.; **Cristalli, G.**
CS Inst. Pharmakologie Toxikologie, Univ. Wuerzburg, Versbacher Str. 9, D-97078 Wuerzburg, Germany
SO Naunyn-Schmiedeberg's Archives of Pharmacology, (1998) Vol. 357, No. 4 SUPPL, pp. R32. print.
Meeting Info.: 39th Spring Meeting of the German Society for Experimental and Clinical Pharmacology and Toxicology. Mainz, Germany. March 17-19, 1998. German Society for Experimental and Clinical Pharmacology and

Toxicology.
CODEN: NSAPCC. ISSN: 0028-1298.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 8 Jul 1998
Last Updated on STN: 8 Jul 1998
IT Major Concepts
Biochemistry and Molecular Biophysics; Membranes (Cell Biology)
IT Parts, Structures, & Systems of Organisms
membrane
IT Chemicals & Biochemicals
adenosine derivative: A-3 adenosine receptor agonist, radioligand; A-3 adenosine receptor

L7 ANSWER 17 OF 18 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 1998:291787 BIOSIS
DN PREV199800291787
TI Novel trisubstituted **adenosine**-uronamides as potential agonist at **A3 adenosine receptor.**
AU Volpini, R. [Reprint author]; Vittori, S. [Reprint author]; Costanzi, S. [Reprint author]; Camaioni, E. [Reprint author]; Baraldi, G.; Jacobson, K. A.; **Cristalli, G.** [Reprint author]
CS Dip. Sci. Chim., Univ. Camerino, I-62032 Camerino, Italy
SO Drug Development Research, (Jan., 1998) Vol. 43, No. 1, pp. 31. print.
Meeting Info.: 6th International Symposium on Adenosine and Adenine Nucleotides: New Frontiers in the 3rd Millennium. Ferrara, Italy. May 19-24, 1998.
CODEN: DDREDK. ISSN: 0272-4391.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 8 Jul 1998
Last Updated on STN: 13 Aug 1998
IT Major Concepts
Pharmacology
IT Chemicals & Biochemicals
adenosine uronamides agonists; adenosine A-3 receptor

L7 ANSWER 18 OF 18 MEDLINE on STN DUPLICATE 15
AN 95222528 MEDLINE
DN PubMed ID: 7707320
TI Search for new purine- and ribose-modified adenosine analogues as selective agonists and antagonists at adenosine receptors.
AU Siddiqi S M; Jacobson K A; Esker J L; Olah M E; Ji X D; Melman N; Tiwari K N; Secrist J A 3rd; Schneller S W; **Cristalli G**; +
CS Molecular Recognition Section, National Institute of Diabetes, and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, Maryland 20892-0810, USA.
NC NO1-AI-72645 (NIAID)
SO Journal of medicinal chemistry, (1995 Mar 31) 38 (7) 1174-88.
Journal code: 9716531. ISSN: 0022-2623.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199505
ED Entered STN: 19950518
Last Updated on STN: 19980206

Entered Medline: 19950511

AB The binding affinities at rat A1, A2a, and **A3 adenosine receptors** of a wide range of derivatives of **adenosine** have been determined. Sites of modification include the purine moiety (1-, 3-, and 7-deaza; halo, alkyne, and amino substitutions at the 2- and 8-positions; and N6-CH2-ring, -hydrazino, and -hydroxylamino) and the ribose moiety (2'-, 3'-, and 5'-deoxy; 2'- and 3'- O-methyl; 2'-deoxy 2'-fluoro; 6'-thio; 5'-uronamide; carbocyclic; 4'- or 3'-methyl; and inversion of configuration). (-)- and (+)-5'-Noraristeromycin were 48- and 21-fold selective, respectively, for A2a vs A1 **receptors.** 2-Chloro-6'-thioadenosine displayed a Ki value of 20 nM at A2a **receptors** (15-fold selective vs A1). 2-Chloroadenin-9-yl(beta-L-2'-deoxy-6'- thiolyxofuranoside) displayed a Ki value of 8 microM at A1 **receptors** and appeared to be an antagonist, on the basis of the absence of a GTP-induced shift in binding vs a radiolabeled antagonist (8-cyclopentyl-1,3-dipropyl-xanthine). 2-Chloro-2'-deoxyadenosine and 2-chloroadenin-9-yl(beta-D-6'-thioarabinoside) were putative partial agonists at A1 **receptors**, with Ki values of 7.4 and 5.4 microM, respectively. The A2a selective agonist 2-(1-hexynyl)-5'-(N-ethylcarbamoyl)**adenosine** displayed a Ki value of 26 nM at **A3 receptors.** The 4'-methyl substitution of **adenosine** was poorly tolerated, yet when combined with other favorable modifications, potency was restored. Thus, N6-benzyl-4'-methyladenosine-5'-(N-methyluronamide) displayed a Ki value of 604 nM at **A3 receptors** and was 103- and 88-fold selective vs A1 and A2a **receptors**, respectively. This compound was a full agonist in the **A3**-mediated inhibition of adenylate cyclase in transfected CHO cells. The carbocyclic analogue of N6-(3-iodobenzyl) **adenosine**-5'-(N-methyluronamide) was 2-fold selective for **A3** vs A1 **receptors** and was nearly inactive at A2a **receptors.**

CT Check Tags: In Vitro; Support, U.S. Gov't, P.H.S.
*Adenosine: AA, analogs & derivatives
Animals
CHO Cells
Cell Membrane: ME, metabolism
Corpus Striatum: ME, metabolism
Hamsters
Magnetic Resonance Spectroscopy
Purines: CH, chemistry
Radioligand Assay
Rats
*Receptors, Purinergic P1: AG, agonists
*Receptors, Purinergic P1: AI, antagonists & inhibitors
Recombinant Proteins
Ribose: CH, chemistry
Structure-Activity Relationship

=>

Structure Search

Eric Crane 10/657,762

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DICTIONARY FILE UPDATES:  29 SEP 2004  HIGHEST RN 754169-63-6

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L1                STR
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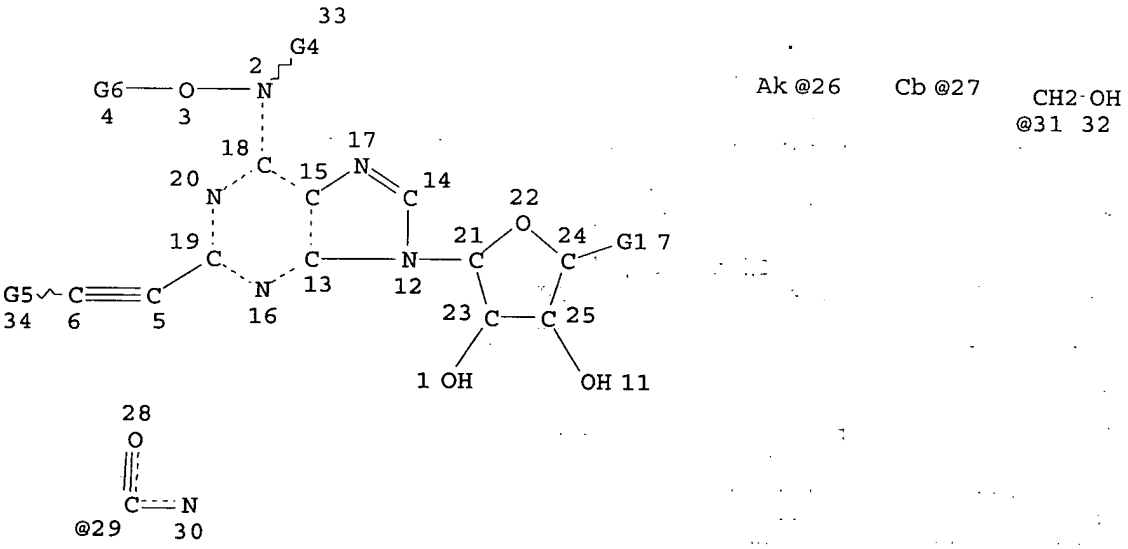


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VAR G5=H/AK/CY/SI
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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
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FILE LAST UPDATED: 29 Sep 2004  (20040929/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

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L2           52 SEA FILE=REGISTRY SSS FUL L1
L3            1 SEA FILE=CAPLUS ABB=ON  PLU=ON  L2


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L3   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         2004:220345  CAPLUS
DOCUMENT NUMBER:          140:264531
TITLE:                    Adenosine A3 receptor agonists
INVENTOR(S):              Cristalli, Gloria
PATENT ASSIGNEE(S):       Cv Therapeutics, Inc., USA
SOURCE:                   PCT Int. Appl., 44 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.        DATE
     ---------------      ----   --------    --------------------   --------
     WO 2004022573         A2    20040318    WO 2003-US28025        20030908
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WO 2004022573 A3 20040408
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2004121978 A1 20040624 US 2003-657762 20030908
PRIORITY APPLN. INFO.: US 2002-409424P P 20020909
OTHER SOURCE(S): MARPAT 140:264531

Priority

AB Adenosine A3 receptor agonists, useful for treating various disease states, including neurol. and cardiac ischemia, asthma, leukopenia and neutropenia, cancer and inflammation, are described. For example, (4S,2R,3R,5R)-5-(hydroxymethyl)-2-[6-(methoxyamino)]-2-[(2-(4-methylphenyl)ethenyl)purin-9-yl]oxolane-3,4-diol was prepared and tested for its affinity for human A1, A2 and A3 adenosine receptors in HEK-293 or CHO cells. The compound demonstrated to be A3 adenosine receptor agonist.

IC ICM C07H019-00

CC 1-12 (Pharmacology)
Section cross-reference(s): 28, 63

IT **672299-04-6P 672299-05-7P 672299-06-8P**
672299-07-9P 672299-08-0P 672299-09-1P
672299-10-4P 672299-11-5P 672299-12-6P
672299-13-7P 672299-14-8P 672299-15-9P
672299-23-9P 672299-24-0P 672299-25-1P
672299-26-2P 672299-27-3P 672299-28-4P
672299-29-5P 672299-30-8P 672299-31-9P
672299-32-0P 672299-33-1P 672299-34-2P
672299-35-3P 672299-36-4P 672299-37-5P
672299-38-6P 672299-39-7P 672299-40-0P
672299-41-1P 672299-42-2P 672299-43-3P
672299-44-4P 672299-45-5P 672299-46-6P
672299-47-7P 672299-48-8P 672299-49-9P
672299-50-2P 672299-51-3P 672299-52-4P
672299-53-5P 672299-54-6P 672299-55-7P
672299-56-8P 672299-57-9P 672299-58-0P
672299-59-1P 672299-60-4P 672299-61-5P
672299-62-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation, compns. and therapeutic uses of adenosine A3 receptor agonists)

IT **672299-04-6P 672299-05-7P 672299-06-8P**
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672299-10-4P 672299-11-5P 672299-12-6P
672299-13-7P 672299-14-8P 672299-15-9P
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672299-44-4P 672299-45-5P 672299-46-6P

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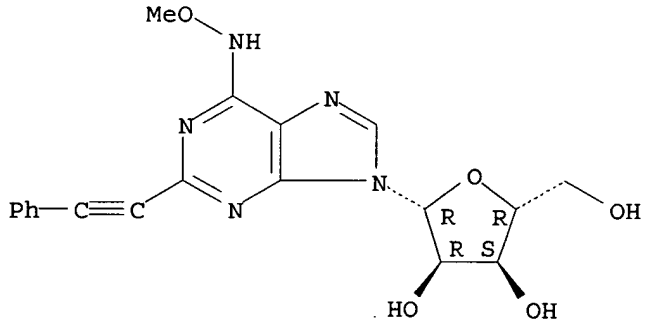
672299-53-5P 672299-54-6P 672299-55-7P
672299-56-8P 672299-57-9P 672299-58-0P
672299-59-1P 672299-60-4P 672299-61-5P
672299-62-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation, compns. and therapeutic uses of adenosine A3 receptor agonists)

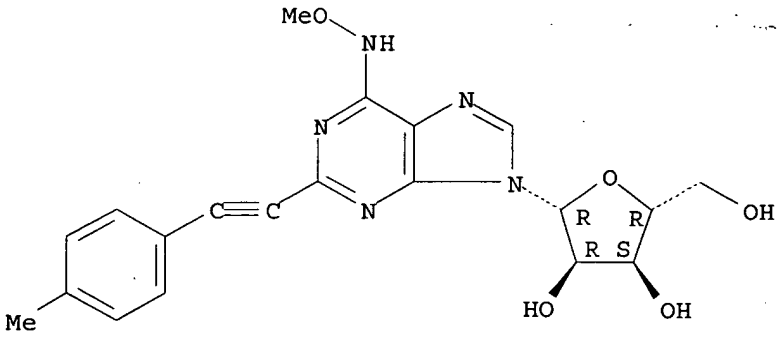
RN 672299-04-6 CAPLUS
CN Inosine, 2-(phenylethynyl)-, O-methyloxime (9CI) (CA INDEX NAME)

Absolute stereochemistry.



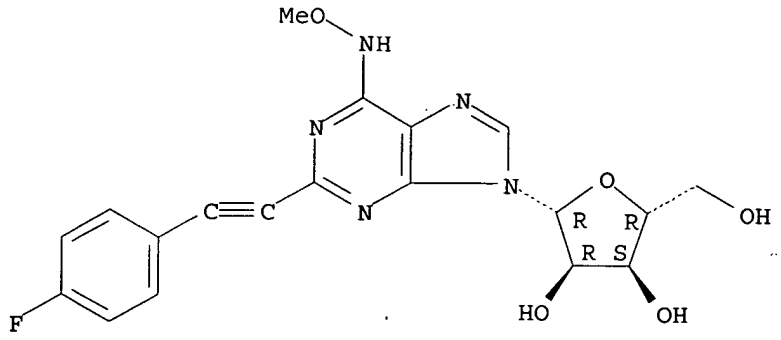
RN 672299-05-7 CAPLUS
CN Inosine, 2-[(4-methylphenyl)ethynyl]-, O-methyloxime (9CI) (CA INDEX NAME)

Absolute stereochemistry.



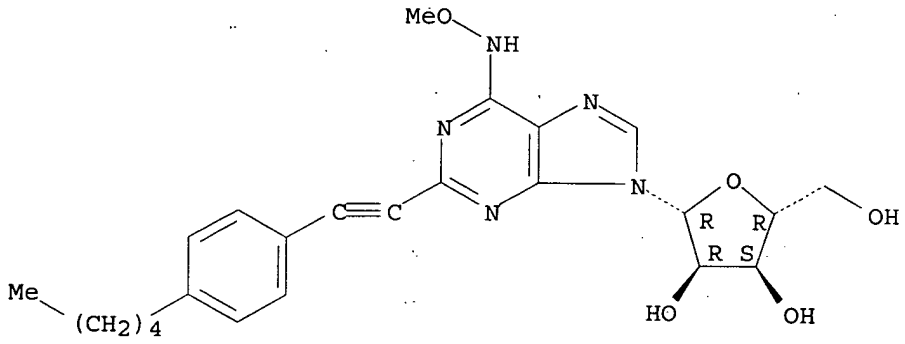
RN 672299-06-8 CAPLUS
CN Inosine, 2-[(4-fluorophenyl)ethynyl]-, O-methyloxime (9CI) (CA INDEX NAME)

Absolute stereochemistry.



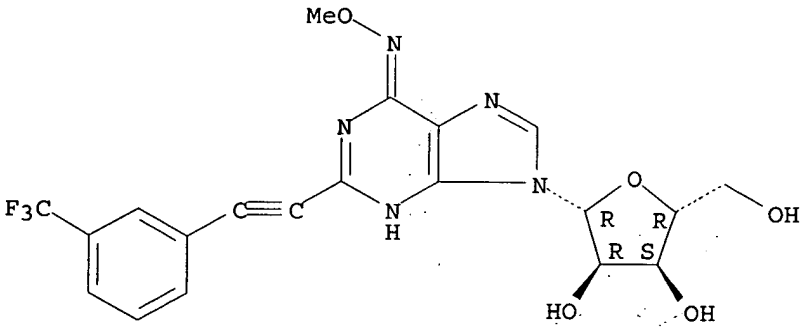
RN 672299-07-9 CAPLUS
CN Inosine, 2-[(4-pentylphenyl)ethynyl]-, O-methyloxime (9CI) (CA INDEX NAME)

Absolute stereochemistry.



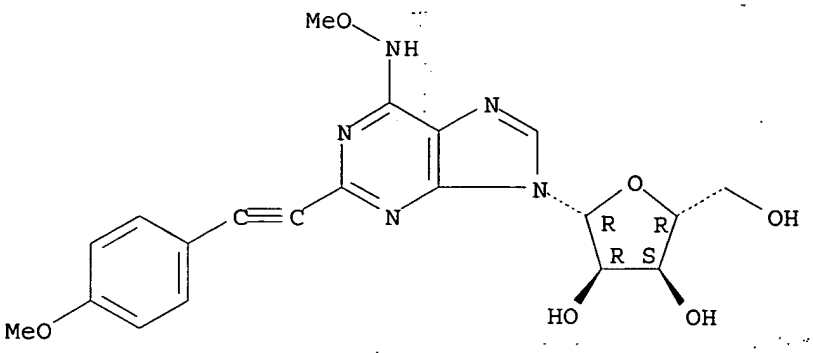
RN 672299-08-0 CAPLUS
CN Inosine, 2-[[3-(trifluoromethyl)phenyl]ethynyl]-, O-methyloxime (9CI) (CA INDEX NAME)

Absolute stereochemistry.



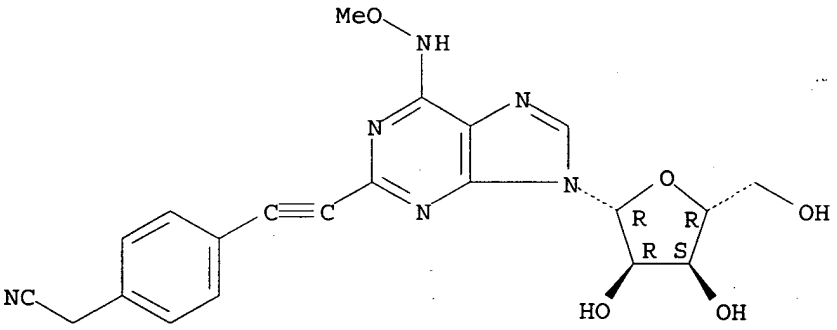
RN 672299-09-1 CAPLUS
CN Inosine, 2-[(4-methoxyphenyl)ethynyl]-, O-methyloxime (9CI) (CA INDEX NAME)

Absolute stereochemistry.



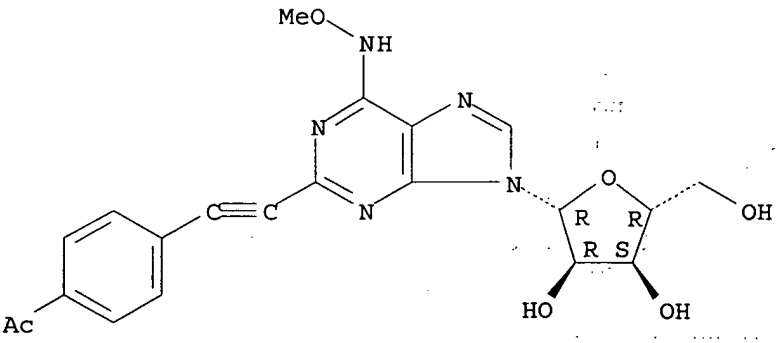
RN 672299-10-4 CAPLUS
CN Inosine, 2-[[4-(cyanomethyl)phenyl]ethynyl]-, O-methyloxime (9CI) (CA INDEX NAME)

Absolute stereochemistry.



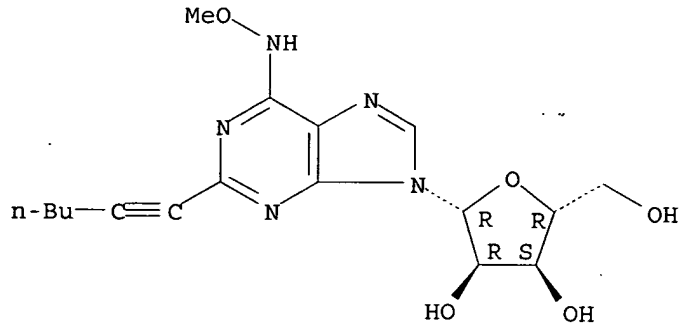
RN 672299-11-5 CAPLUS
CN Inosine, 2-[(4-acetylphenyl)ethynyl]-, 6-(O-methyloxime) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



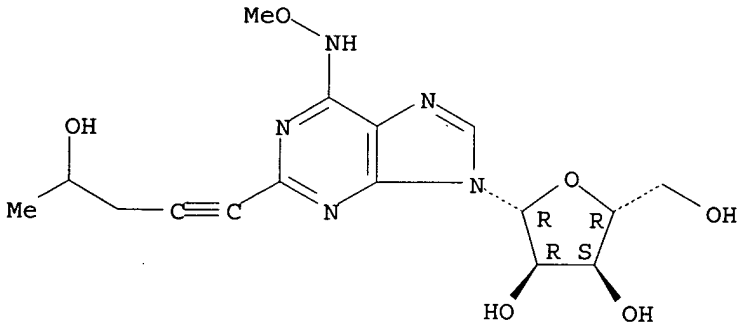
RN 672299-12-6 CAPLUS
CN Inosine, 2-(1-hexynyl)-, O-methyloxime (9CI) (CA INDEX NAME)

Absolute stereochemistry.



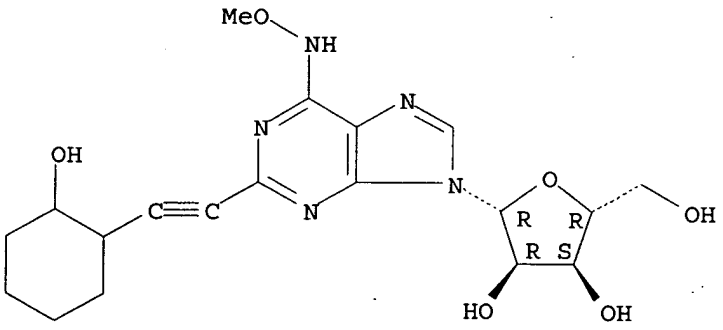
RN 672299-13-7 CAPLUS
CN Inosine, 2-(4-hydroxy-1-pentynyl)-, O-methyloxime (9CI) (CA INDEX NAME)

Absolute stereochemistry.



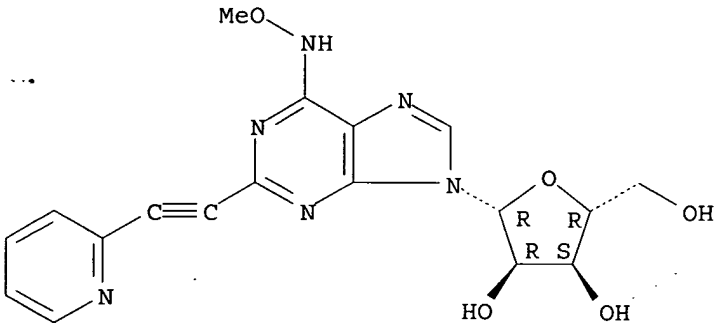
RN 672299-14-8 CAPLUS
CN Inosine, 2-[(2-hydroxycyclohexyl)ethynyl]-, O-methyloxime (9CI) (CA INDEX NAME)

Absolute stereochemistry.



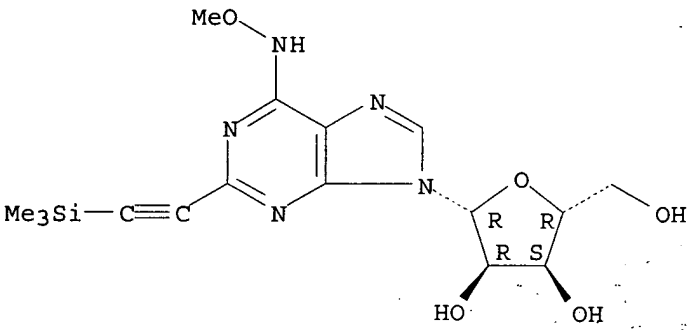
RN 672299-15-9 CAPLUS
CN Inosine, 2-(2-pyridinylethynyl)-, O-methyloxime (9CI) (CA INDEX NAME)

Absolute stereochemistry.



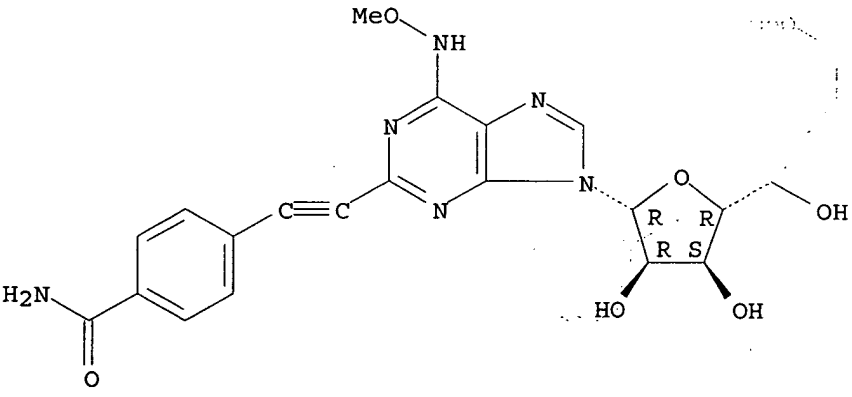
RN 672299-23-9 CAPLUS
CN Inosine, 2-[(trimethylsilyl)ethynyl]-, O-methyloxime (9CI) (CA INDEX NAME)

Absolute stereochemistry.



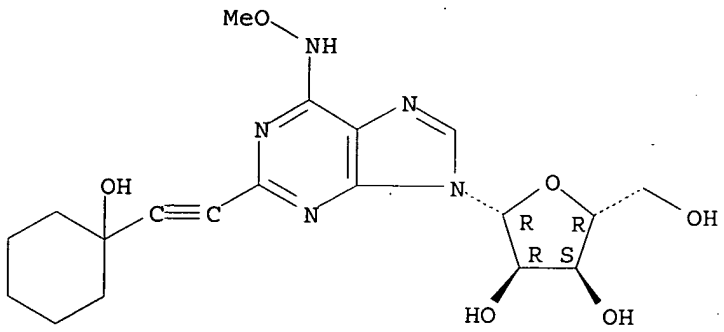
RN 672299-24-0 CAPLUS
CN Inosine, 2-[[4-(aminocarbonyl)phenyl]ethynyl]-, 6-(O-methyloxime) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



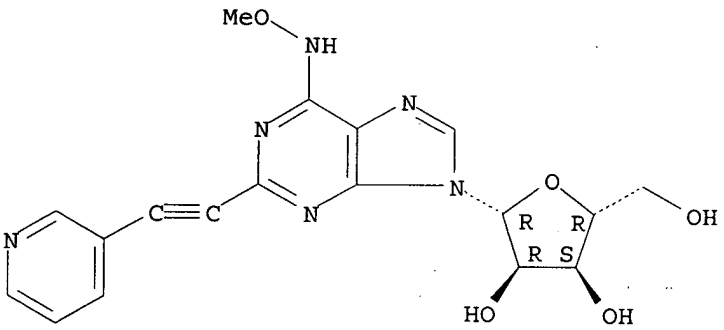
RN 672299-25-1 CAPLUS
CN Inosine, 2-[(1-hydroxycyclohexyl)ethynyl]-, O-methyloxime (9CI) (CA INDEX NAME)

Absolute stereochemistry.



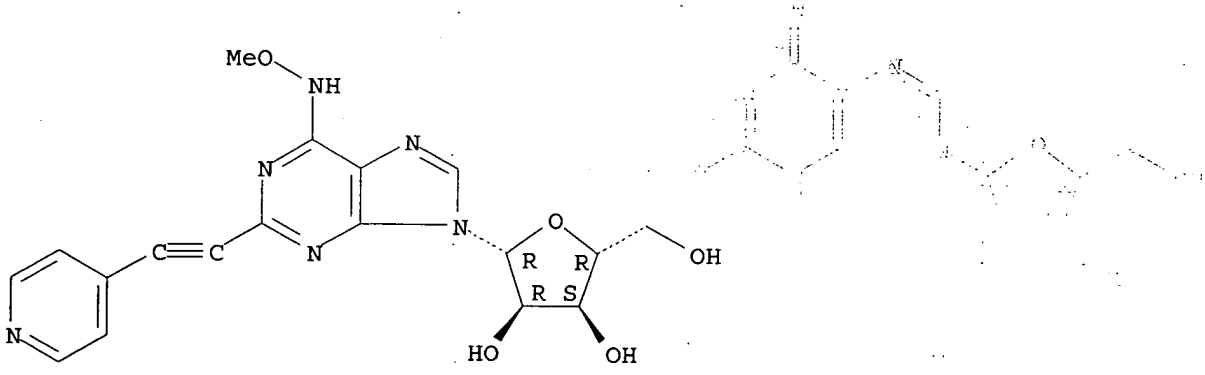
RN 672299-26-2 CAPLUS
CN Inosine, 2-(3-pyridinylethynyl)-, O-methyloxime (9CI) (CA INDEX NAME)

Absolute stereochemistry.



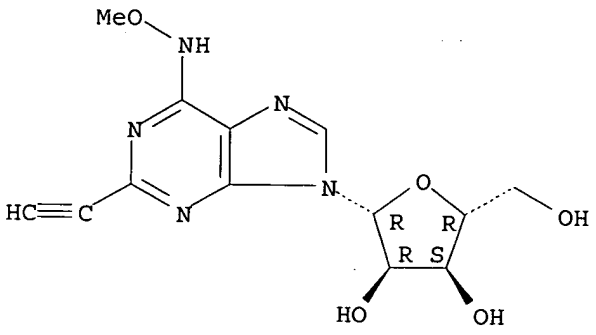
RN 672299-27-3 CAPLUS
CN Inosine, 2-(4-pyridinylethynyl)-, O-methyloxime (9CI) (CA INDEX NAME)

Absolute stereochemistry.



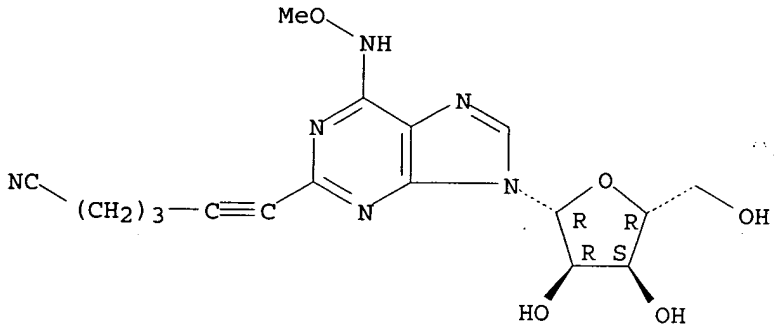
RN 672299-28-4 CAPLUS
CN Inosine, 2-ethynyl-, O-methyloxime (9CI) (CA INDEX NAME)

Absolute stereochemistry.



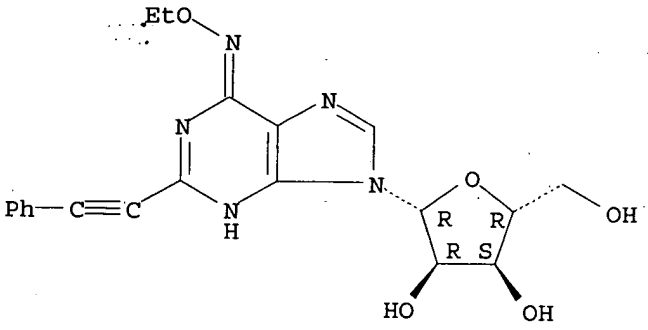
RN 672299-29-5 CAPLUS
CN Inosine, 2-(5-cyano-1-pentynyl)-, O-methyloxime (9CI) (CA INDEX NAME)

Absolute stereochemistry.



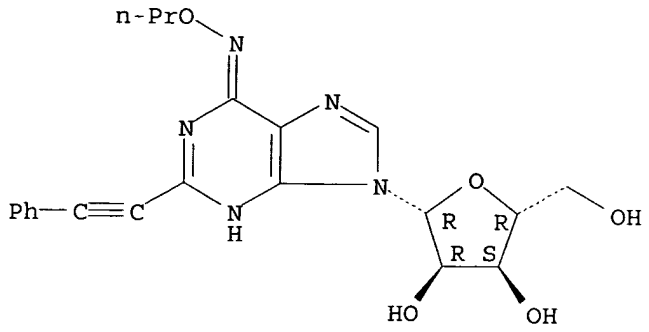
RN 672299-30-8 CAPLUS
CN Inosine, 2-(phenylethynyl)-, O-ethyloxime (9CI) (CA INDEX NAME)

Absolute stereochemistry.



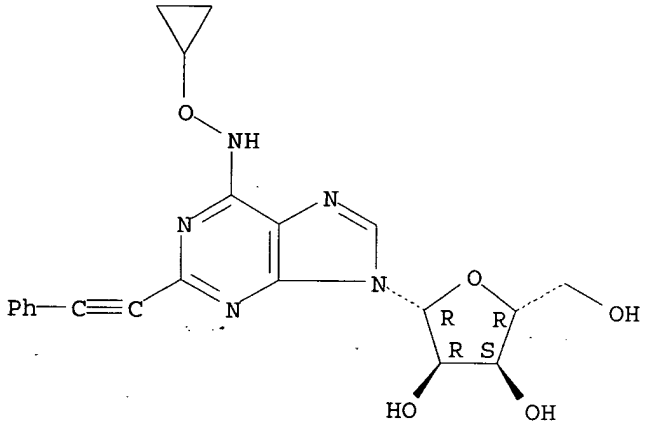
RN 672299-31-9 CAPLUS
CN Inosine, 2-(phenylethynyl)-, O-propyloxime (9CI) (CA INDEX NAME)

Absolute stereochemistry.



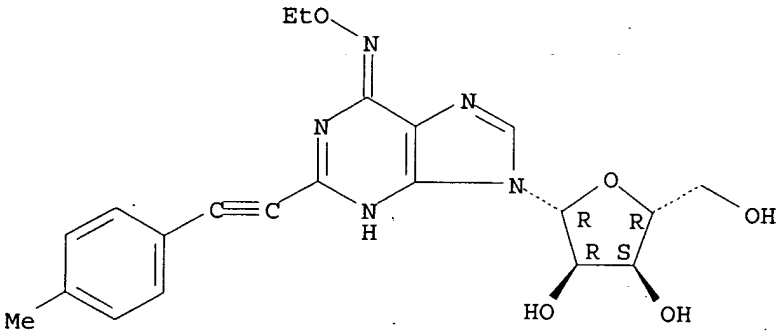
RN 672299-32-0 CAPLUS
CN Inosine, 2-(phenylethynyl)-, O-cyclopropyloxime (9CI) (CA INDEX NAME)

Absolute stereochemistry.



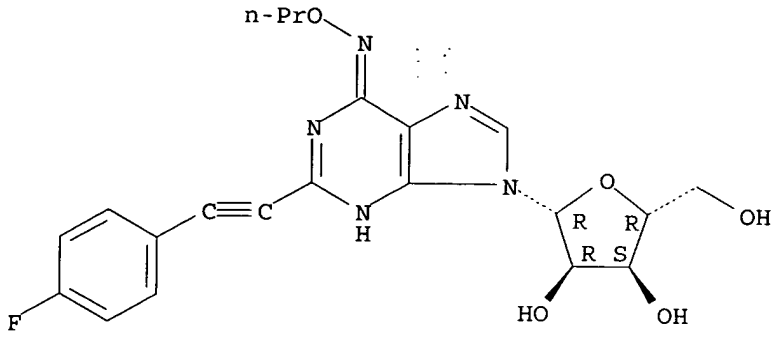
RN 672299-33-1 CAPLUS
CN Inosine, 2-[(4-methylphenyl)ethynyl]-, O-ethyloxime (9CI) (CA INDEX NAME)

Absolute stereochemistry.



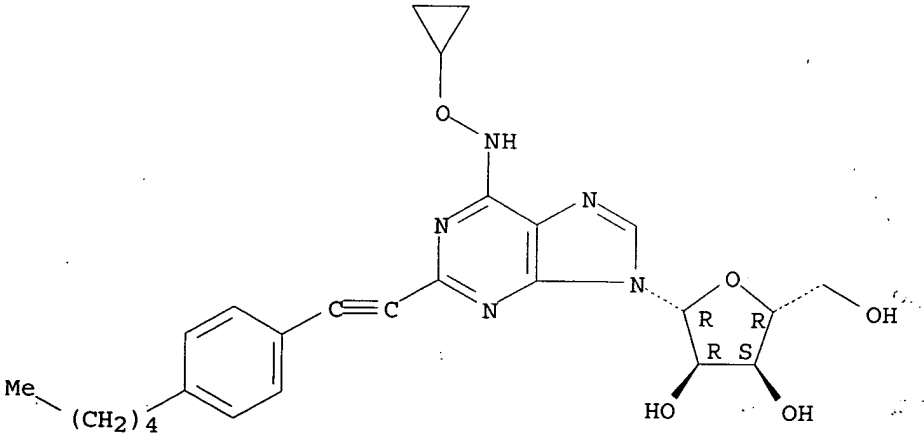
RN 672299-34-2 CAPLUS
CN Inosine, 2-[(4-fluorophenyl)ethynyl]-, O-propyloxime (9CI) (CA INDEX NAME)

Absolute stereochemistry.



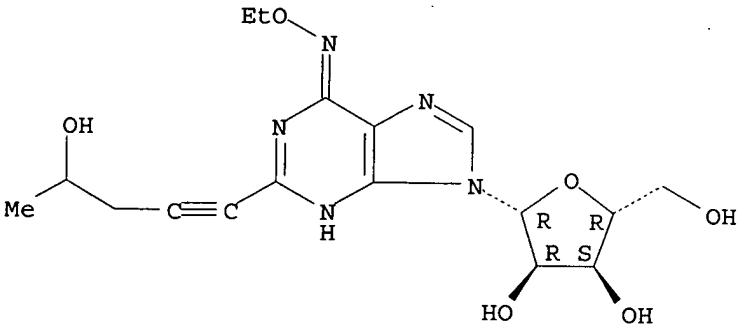
RN 672299-35-3 CAPLUS
CN Inosine, 2-[(4-pentylphenyl)ethynyl]-, O-cyclopropyloxime (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 672299-36-4 CAPLUS
CN Inosine, 2-(4-hydroxy-1-pentynyl)-, O-ethyloxime (9CI) (CA INDEX NAME)

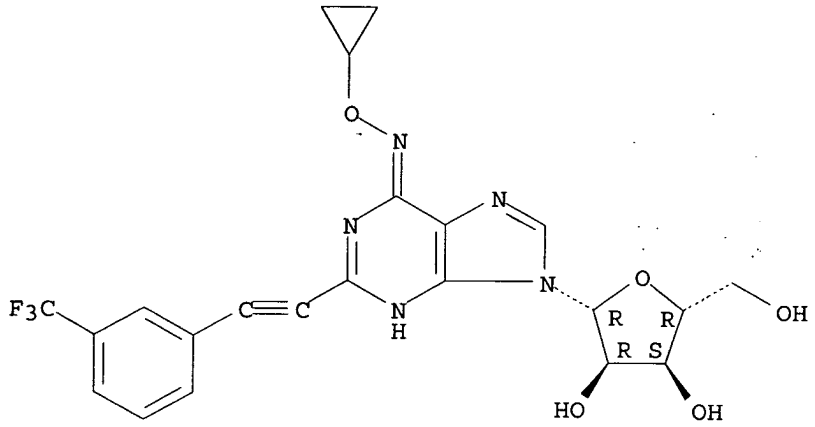
Absolute stereochemistry.



RN 672299-37-5 CAPLUS

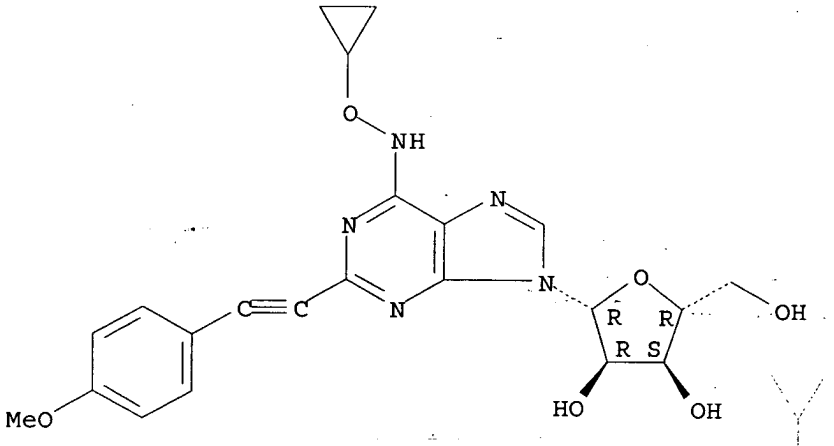
CN Inosine, 2-[[3-(trifluoromethyl)phenyl]ethynyl]-, O-cyclopropyloxime (9CI) (CA INDEX NAME)

Absolute stereochemistry.



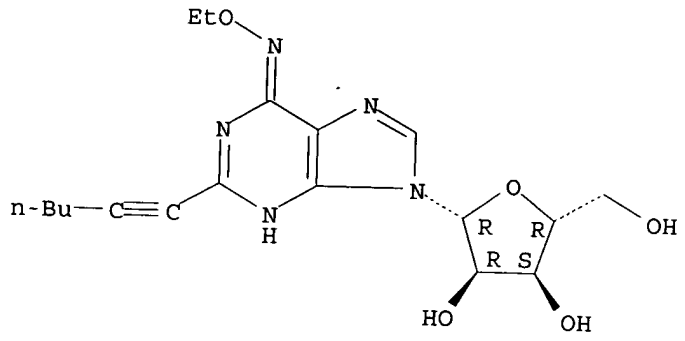
RN 672299-38-6 CAPLUS
CN Inosine, 2-[(4-methoxyphenyl)ethynyl]-, O-cyclopropyloxime (9CI) (CA INDEX NAME)

Absolute stereochemistry.



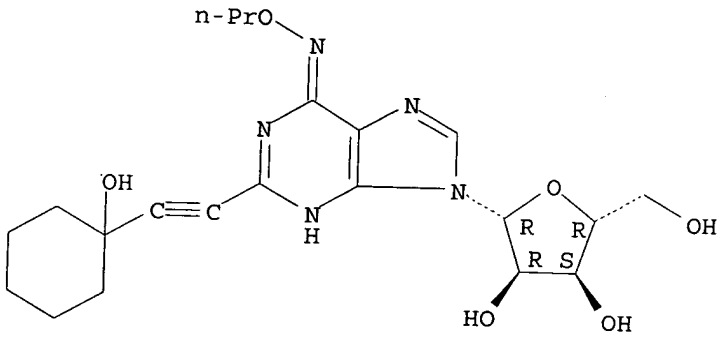
RN 672299-39-7 CAPLUS
CN Inosine, 2-(1-hexynyl)-, O-ethyloxime (9CI) (CA INDEX NAME)

Absolute stereochemistry.



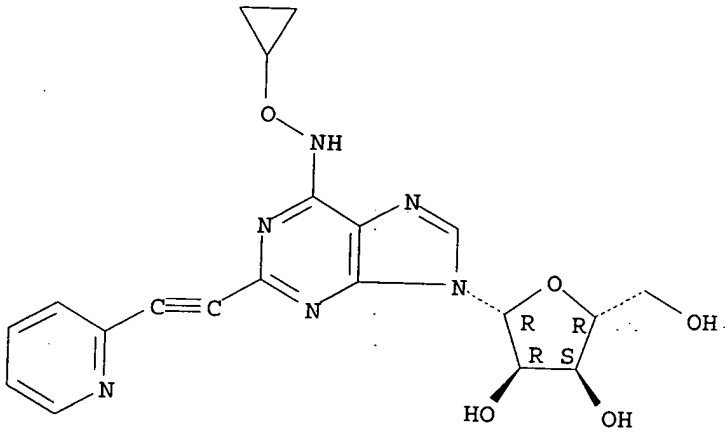
RN 672299-40-0 CAPLUS
CN Inosine, 2-[(1-hydroxycyclohexyl)ethynyl]-, O-propyloxime (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 672299-41-1 CAPLUS
CN Inosine, 2-(2-pyridinylethynyl)-, O-cyclopropyloxime (9CI) (CA INDEX NAME)

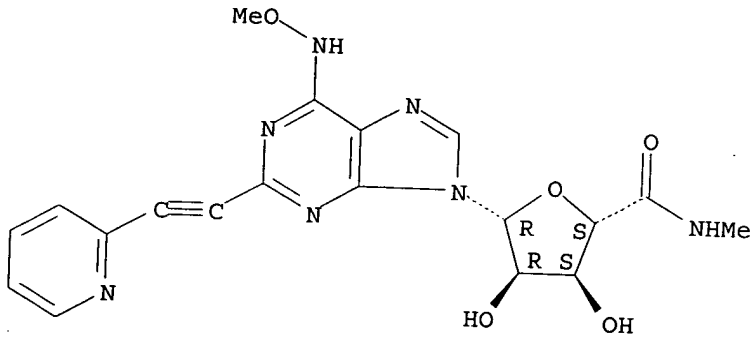
Absolute stereochemistry.



RN 672299-42-2 CAPLUS
CN β-D-Ribofuranuronamide, 1-deoxy-1-[6-(methoxyamino)-2-(2-

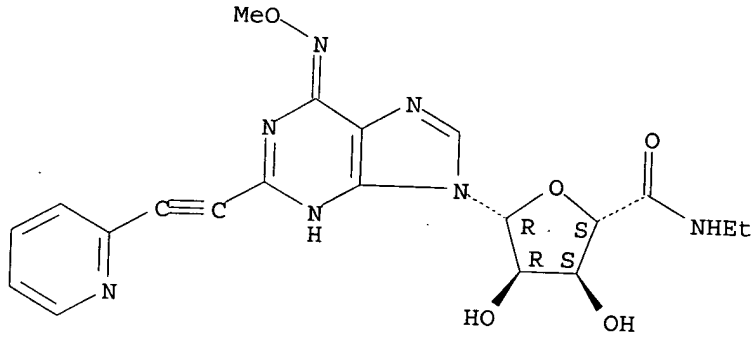
pyridinylethynyl)-9H-purin-9-yl]-N-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



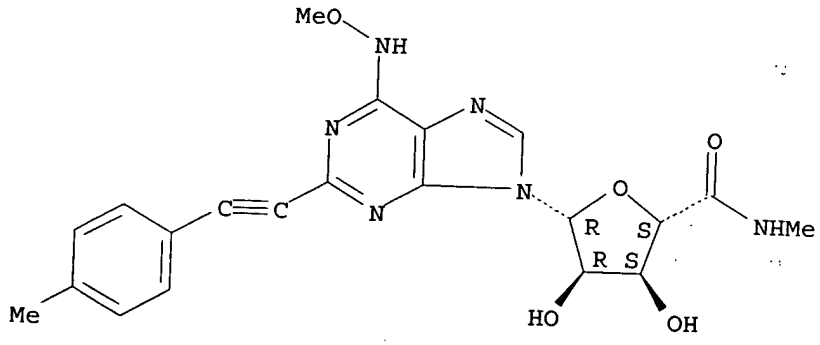
RN 672299-43-3 CAPLUS
CN β-D-Ribofuranuronamide, 1-deoxy-N-ethyl-1-[6-(methoxyamino)-2-(2-pyridinylethynyl)-9H-purin-9-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 672299-44-4 CAPLUS
CN β-D-Ribofuranuronamide, 1-deoxy-1-[6-(methoxyamino)-2-[(4-methylphenyl)ethynyl]-9H-purin-9-yl]-N-methyl- (9CI) (CA INDEX NAME)

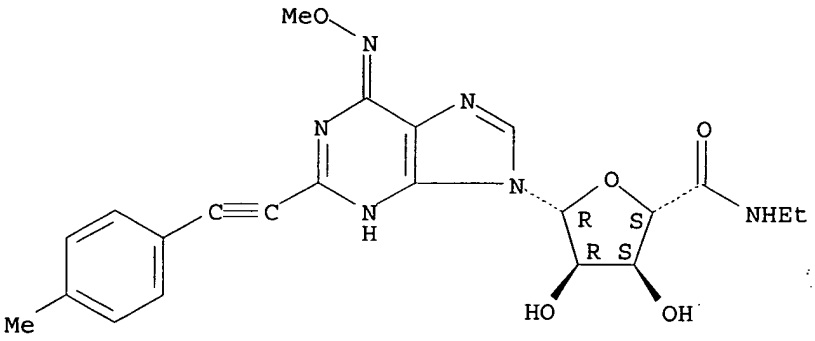
Absolute stereochemistry.



RN 672299-45-5 CAPLUS
CN β-D-Ribofuranuronamide, 1-deoxy-N-ethyl-1-[6-(methoxyamino)-2-[(4-

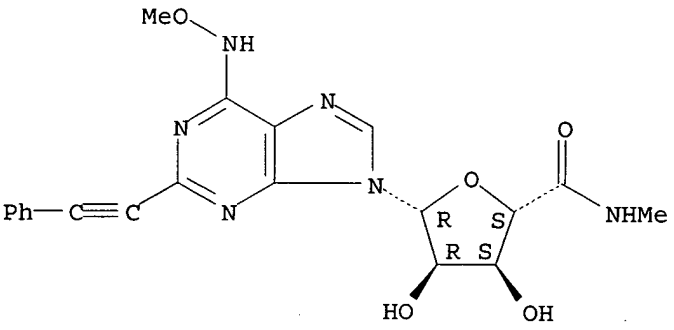
methylphenyl)ethynyl]-9H-purin-9-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



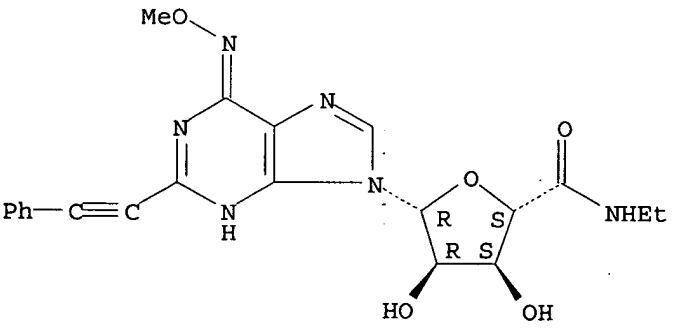
RN 672299-46-6 CAPLUS
CN β-D-Ribofuranuronamide, 1-deoxy-1-[6-(methoxyamino)-2-(phenylethynyl)-9H-purin-9-yl]-N-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 672299-47-7 CAPLUS
CN β-D-Ribofuranuronamide, 1-deoxy-N-ethyl-1-[6-(methoxyamino)-2-(phenylethynyl)-9H-purin-9-yl]- (9CI) (CA INDEX NAME)

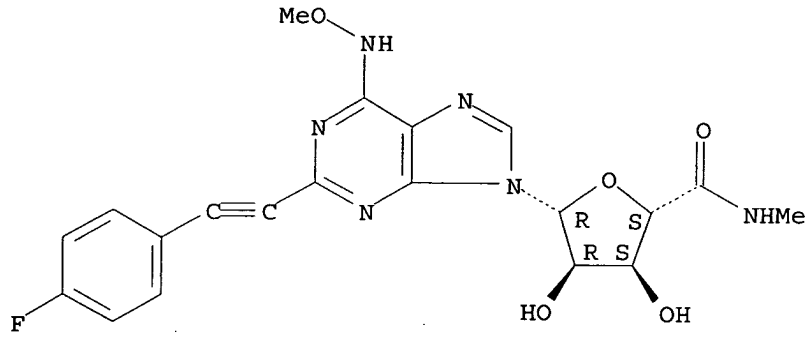
Absolute stereochemistry.



RN 672299-48-8 CAPLUS
CN β-D-Ribofuranuronamide, 1-deoxy-1-[2-[(4-fluorophenyl)ethynyl]-6-

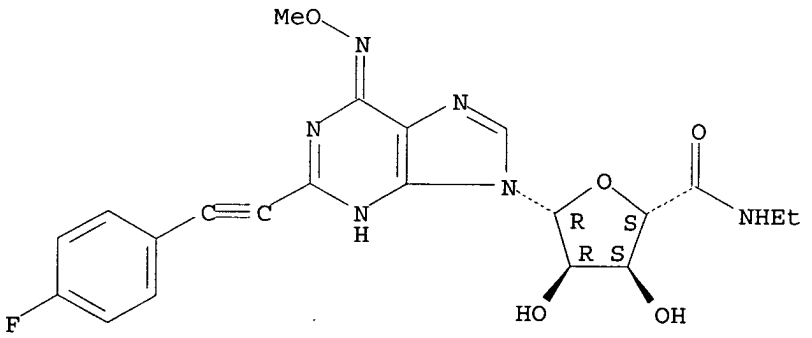
(methoxyamino)-9H-purin-9-yl]-N-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



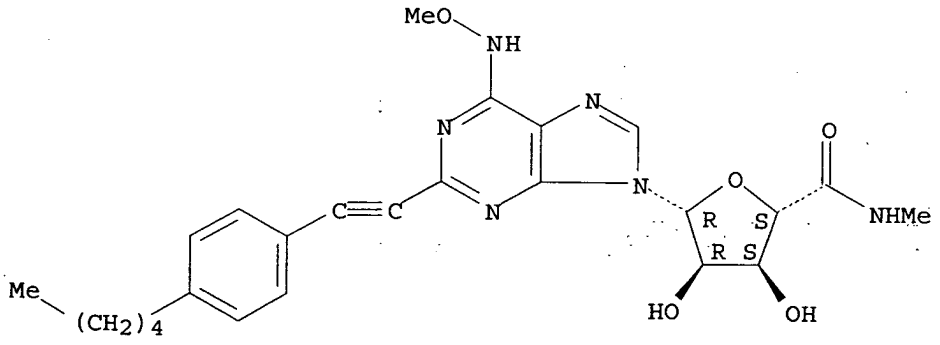
RN 672299-49-9 CAPLUS
CN β-D-Ribofuranuronamide, 1-deoxy-N-ethyl-1-[2-[(4-fluorophenyl)ethynyl]-6-(methoxyamino)-9H-purin-9-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 672299-50-2 CAPLUS
CN β-D-Ribofuranuronamide, 1-deoxy-1-[6-(methoxyamino)-2-[(4-pentylphenyl)ethynyl]-9H-purin-9-yl]-N-methyl- (9CI) (CA INDEX NAME)

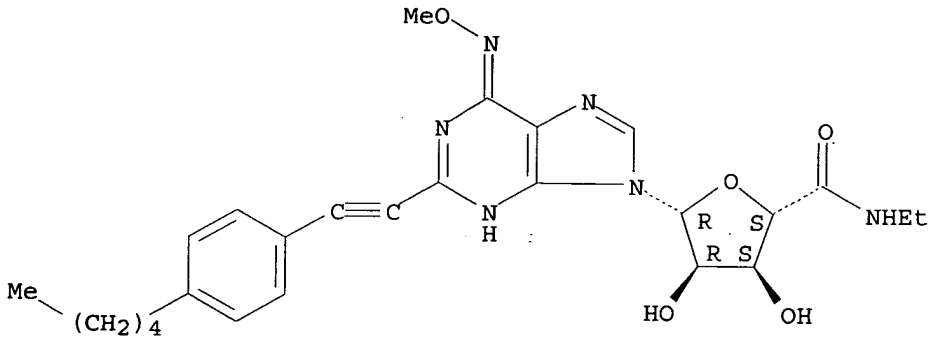
Absolute stereochemistry.



RN 672299-51-3 CAPLUS

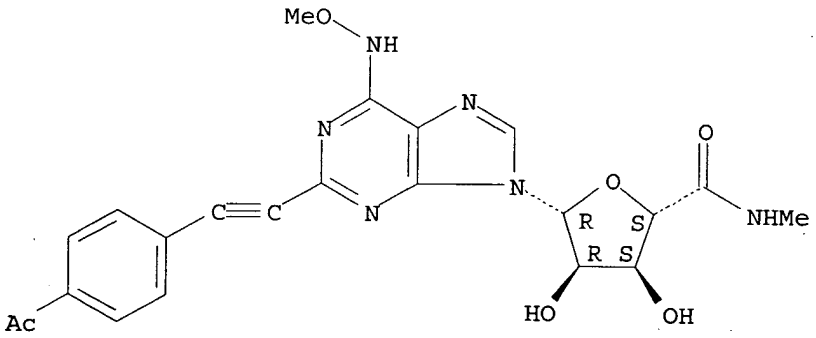
CN β-D-Ribofuranuronamide, 1-deoxy-N-ethyl-1-[6-(methoxyamino)-2-[(4-pentylphenyl)ethynyl]-9H-purin-9-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



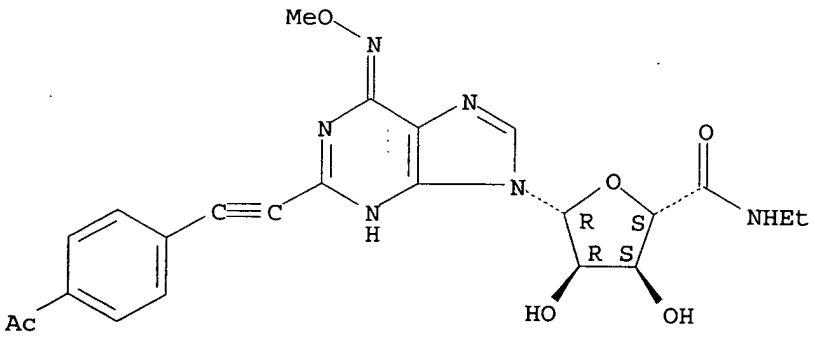
RN 672299-52-4 CAPLUS
CN β-D-Ribofuranuronamide, 1-[2-[(4-acetylphenyl)ethynyl]-6-(methoxyamino)-9H-purin-9-yl]-1-deoxy-N-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 672299-53-5 CAPLUS
CN β-D-Ribofuranuronamide, 1-[2-[(4-acetylphenyl)ethynyl]-6-(methoxyamino)-9H-purin-9-yl]-1-deoxy-N-ethyl- (9CI) (CA INDEX NAME)

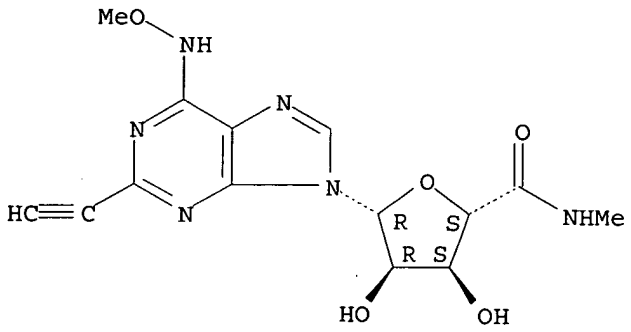
Absolute stereochemistry.



RN 672299-54-6 CAPLUS

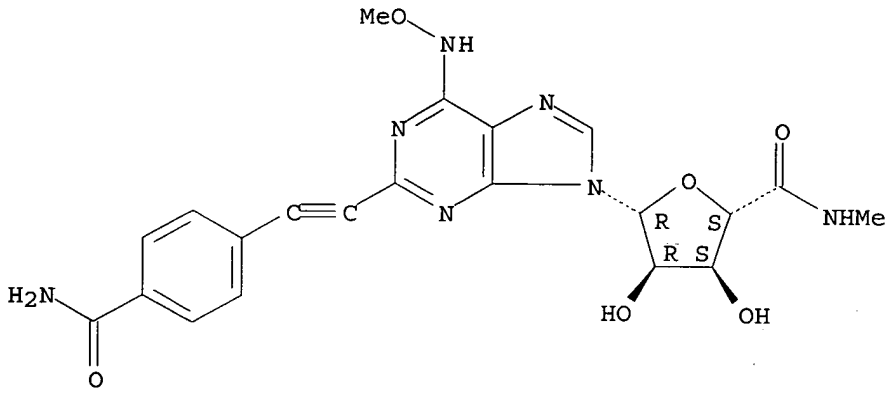
CN β-D-Ribofuranuronamide, 1-deoxy-1-[2-ethynyl-6-(methoxyamino)-9H-purin-9-yl]-N-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



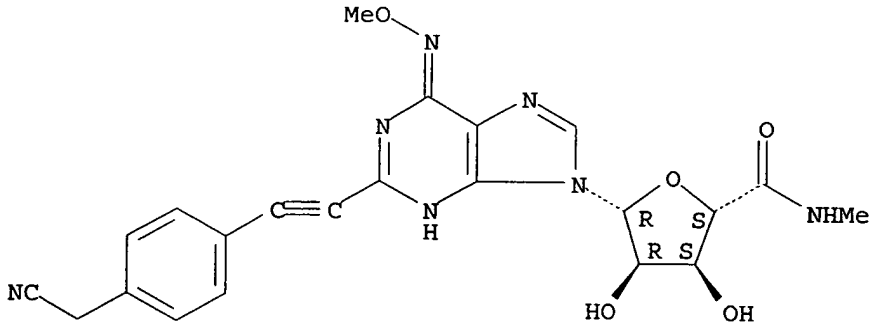
RN 672299-55-7 CAPLUS
CN β-D-Ribofuranuronamide, 1-[2-[[4-(aminocarbonyl)phenyl]ethynyl]-6-(methoxyamino)-9H-purin-9-yl]-1-deoxy-N-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



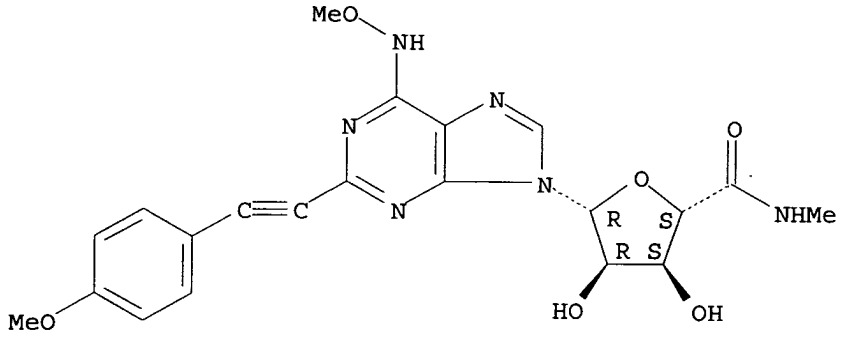
RN 672299-56-8 CAPLUS
CN β-D-Ribofuranuronamide, 1-[2-[[4-(cyanomethyl)phenyl]ethynyl]-6-(methoxyamino)-9H-purin-9-yl]-1-deoxy-N-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



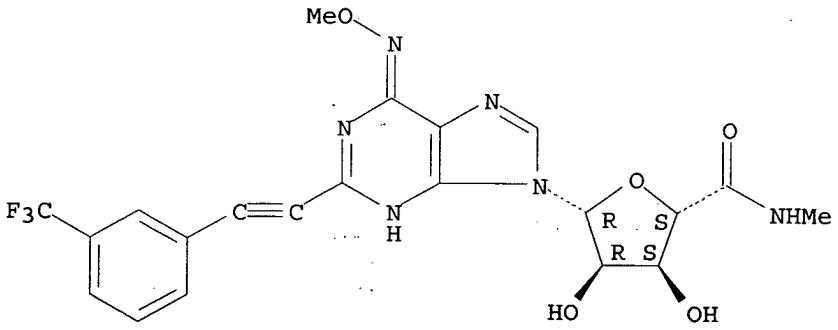
RN 672299-57-9 CAPLUS
CN β-D-Ribofuranuronamide, 1-deoxy-1-[6-(methoxyamino)-2-[(4-methoxyphenyl)ethynyl]-9H-purin-9-yl]-N-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



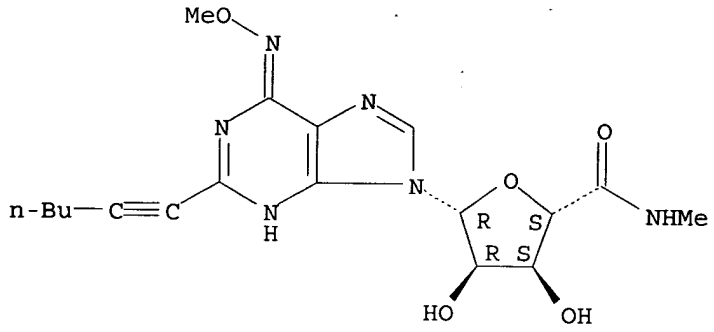
RN 672299-58-0 CAPLUS
CN β-D-Ribofuranuronamide, 1-deoxy-1-[6-(methoxyamino)-2-[[3-(trifluoromethyl)phenyl]ethynyl]-9H-purin-9-yl]-N-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



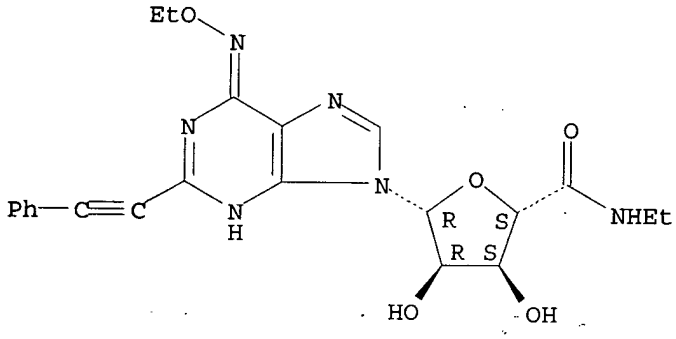
RN 672299-59-1 CAPLUS
CN β-D-Ribofuranuronamide, 1-deoxy-1-[2-(1-hexynyl)-6-(methoxyamino)-9H-purin-9-yl]-N-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



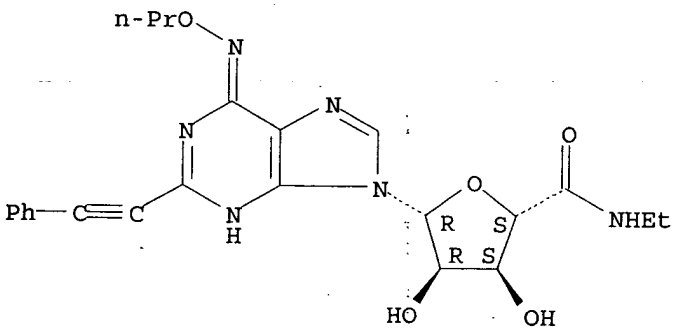
RN 672299-60-4 CAPLUS
CN β-D-Ribofuranuronamide, 1-deoxy-1-[6-(ethoxyamino)-2-(phenylethynyl)-9H-purin-9-yl]-N-ethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



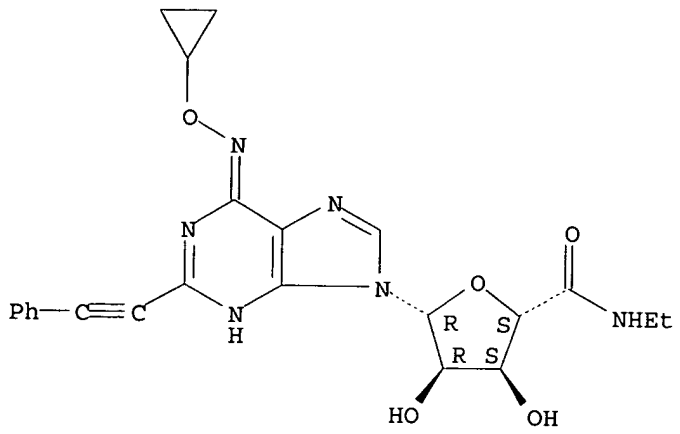
RN 672299-61-5 CAPLUS
CN β-D-Ribofuranuronamide, 1-deoxy-N-ethyl-1-[2-(phenylethynyl)-6-(propoxyamino)-9H-purin-9-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 672299-62-6 CAPLUS
CN β-D-Ribofuranuronamide, 1-[6-[(cyclopropyloxy)amino]-2-(phenylethynyl)-9H-purin-9-yl]-1-deoxy-N-ethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.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